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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,162	06/17/2005	Theodore J Nitz	1282-P02959US01	2828

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EXAMINER	
KOSACK, JOSEPH R	

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
12/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,162	NITZ ET AL.	
	Examiner	Art Unit	
	Joseph R. Kosack	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4 and 6-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4 and 6-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/3/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 4, and 6-35 are pending in the instant application.

Amendments

The amendment filed on August 29, 2008 has been acknowledged and has been entered into the application file.

Information Disclosure Statement

The Information Disclosure Statement filed on September 3, 2008 has been considered by the Examiner.

Previous Claim Rejections - 35 USC § 102

Claims 1, 3, and 11 were previously rejected under 35 U.S.C. 102(b) as being anticipated by Nitz et al. (WO/99/38508 A1).

Applicant's amendments have removed the anticipated subject matter, and the rejection is withdrawn.

Previous Claim Rejections - 35 USC § 103

Claims 1-33 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Nitz et al. (WO/99/38508 A1) in view of DeLuca et al. (*Pharma. Dosage Forms Vol 1: Parenteral Medications, 1992*, 173-175).

The Applicant has traversed the rejection on the grounds that in light of the Takeda v. Alphapharm case and that the claimed compounds have an unexpected property in that they have improved solubility in ethanolic solvents which facilitates the preparation of a composition for EHD spraying.

The Examiner must respectfully disagree. Firstly, the Takeda v. Alphapharm case deals with a prior art compound that would require *two* modifications in order to yield the claimed compound. The instant case requires only one modifcation, namely the movement of the substituent on the central phenyl ring from the para to the meta position. Additionally, the Supreme Court in KSR v. Teleflex state that the reasoning for a modification need not come directly from the references cited, but may come from other sources such as the common skill in the art. The Examiner advanced a reasoning as to why the modification would be attempted and why it would have a reasonable expectation of success.

As to the improved solubility in ethanolic solvents, the Applicant has not shown that this improvement is over the compounds where the substituent on the central phenyl ring is in the para position. Therefore, the supposed improved solubility does not currently carry much weight.

Therefore, Applicant's arguments have been considered, but they are not found to be persuasive in respect to the invention as a whole and the *prima facie* case of obviousness advanced by the Examiner. The rejection is maintained for all claims except claims 2, 3, and 5 as they have been cancelled.

Claims 34-35 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Nitz et al. (WO/99/38508 A1).

The Applicant has traversed the rejection on the grounds that the rejection is improper because R in Scheme A does not include HET and the amendments with

respect to the position of the substituent on the central phenyl ring to yield an improved solubility in ethanolic solvents to further differentiate the claims from the prior art.

The Examiner is not persuaded as the specification teaches a species in which the R group would be pyrdiyl as described in the rejection of the product claims. Additionally, the response to the positional isomer and improved solubility arguments is the same as above for the product claims.

The rejection is maintained, but in a modified form to cover the amendments made by the Applicant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

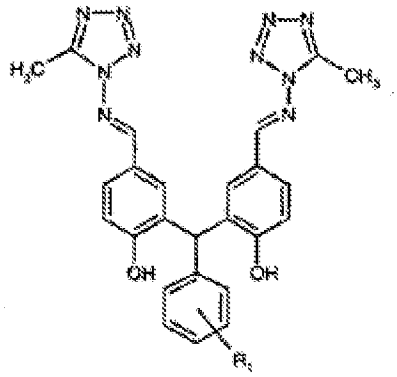
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

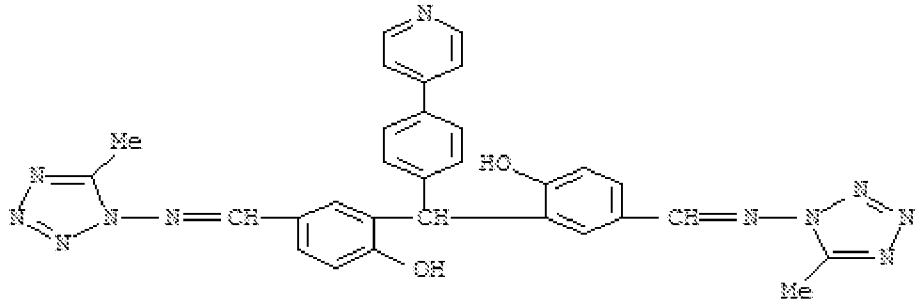
Claims 1, 4, and 6-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nitz et al. (WO/99/38508 A1) in view of DeLuca et al. (*Pharma. Dosage Forms Vol 1: Parenteral Medications, 1992*, 173-175).

The instant claims are drawn to compounds of formula I



with substitutions as defined, compositions comprising compounds of formula I with various amounts of ethanol and water, and methods of use of the compounds of formula I to treat a pneumovirus infection.

Nitz et al. teach the compound



which corresponds to the claims where R1 is pyridine and in the 4-position. See page 27, lines 14-15. Nitz et al. also teach combining the compounds with a pharmaceutically acceptable carrier. See page 10, lines 20-23. Finally, Nitz et al. teach the method of treating pneumovirus infections with the compounds. See page 11, line 8 to page 14, line 10.

Nitz et al. does not teach where R1 is in the 3-position, the quantifies of ethanol, water, etc.. in the composition, and all of the possibilities that R1 can be in the instant application.

DeLuca et al. teach that parenteral formulations usually are aqueous solutions, but in other situations, water may have to be eliminated or reduced to prevent chemical degradation. Additionally, suitable cosolvents such as ethanol and polyethylene glycol. See page 175, Section B. Even though the exact parameters are not taught, one of ordinary skill in the art would be able to determine them through routine optimization.

Additionally, the compound of Nitz et al. is a positional isomer of some of the instantly claimed compounds. The court in In re Norris (84 USPQ 458 (1950)) stated:

The Norris textbook contains the following:

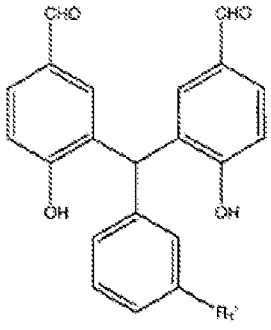
> There are many organic compounds which have the same percentage composition; for example 107 compounds having the

> formula $C_9H_{11}O_2N$ have been described. Such compounds are called isomers (signifying equal measure) and the phenomenon is known as *isomerism.* When two isomers resemble each other closely in chemical properties they are said to be *metameric.* (Italics quoted.)
>
> In view of what has been quoted from the textbook authorities, we think it is conclusively established that structural isomers have defined predictable physical properties, and that the chemical similarity in such a large group justifies the coining of the term "metameric" to characterize such isomeric compounds. The statement made in the Jones case, supra, that isomers possess similar chemical and physical properties is thus shown to have ample basis in the authorities, and that case, as well as the Finley case, supra, are proper precedents to support the rejection of a novel compound which is isomeric with compounds of the prior art, where the new compound is not shown to possess new and unexpected utilities. (citations omitted)

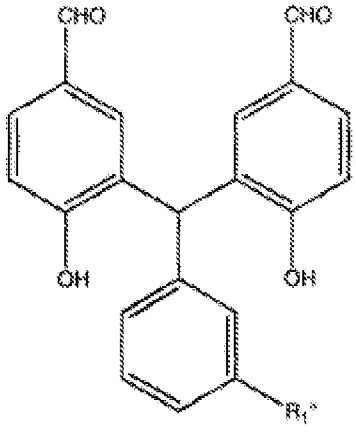
Finally, the court in In re Wood, Whittaker, Stirling, and Ohta (199 USPQ 137) state that compounds with similar structures are expected to have similar properties unless there is evidence on the record of secondary considerations. In the instant case, the same pentacyclic core structure is present between the instant case and Nitz et al., along with evidence of conserved utility when the substituent on the middle phenyl ring is modified. Therefore, one of ordinary skill in the art would expect that putting a different substituent on that phenyl ring will yield another compound capable of treating pneumovirus. Therefore, the claims are *prima facie* obvious over the prior art.

Claims 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nitz et al. (WO/99/38508 A1).

The instant claims are drawn to intermediates of the formulae:

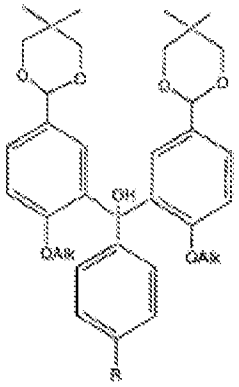


and

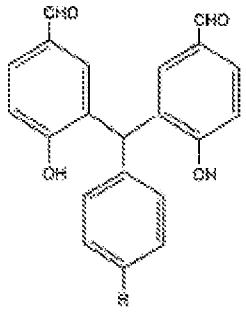


where R1' and R1" are as defined.

Nitz et al. teach compounds of the formulae



and



where R is as defined. See page 7, Scheme A.

Nitz et al. do not specifically teach where R1' and R1" are as defined in the instant claims, nor does Nitz et al. teach where the R group is in the meta position.

Nitz et al. teach a compound where R is pyridine in the final product. By going through Scheme A, compounds which would correspond to where R1' and R1" are HET would be generated. See page 27, lines 14-15.

Additionally, the compound of Nitz et al. is a positional isomer of some of the instantly claimed compounds. The court in In re Norris (84 USPQ 458 (1950)) stated:

> The Norris textbook contains the following:
>
> > There are many organic compounds which have the same percentage composition; for example 107 compounds having the formula $C_9H_{11}O_2N$ have been described. Such compounds are called isomers (signifying equal measure) and the phenomenon is known as *isomerism.* When two isomers resemble each other closely in chemical properties they are said to be *metameric.* (Italics quoted.)
>
> In view of what has been quoted from the textbook authorities, we think it is conclusively established that structural isomers have defined predictable physical properties, and that the chemical similarity in such a large group justifies the coining of the term "metameric" to characterize such isomeric compounds. The statement made in the Jones case, supra, that isomers possess similar chemical and physical properties is thus shown to have ample basis in the authorities, and that case, as well as the Finley case, supra, are proper precedents to support the rejection of a novel compound which is isomeric with compounds of the prior art, where the new compound is not shown to possess new and unexpected utilities. (citations omitted)

Finally, the court in In re Wood, Whittaker, Stirling, and Ohta (199 USPQ 137) state that compounds with similar structures are expected to have similar properties unless there is evidence on the record of secondary considerations. In the instant case, the same pentacyclic core structure is present between the final products in the instant case and the final products in Nitz et al., along with evidence of conserved utility when the substituent on the middle phenyl ring is modified. Therefore, one of ordinary skill in the art would expect that putting a different substituent on that phenyl ring will yield another compound capable of treating pneumovirus.

Therefore, the claims are *prima facie* obvious over the prior art.

Conclusion

Claims 1, 4, and 6-35 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph R. Kosack whose telephone number is (571)272-5575. The examiner can normally be reached on M-Th 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph R Kosack/
Examiner, Art Unit 1626

/REI-TSANG SHIAO /
Primary Examiner, Art Unit 1626